

REMARKS/ARGUMENTS

Claims 1 and 3–10 are pending in the above-captioned application, and all of these claims stand rejected. With this paper, claims 1, 3, 5, 6, and 10 are amended.

I. Claim rejections under 35 U.S.C. § 103(a) as being unpatentable over Stapleton (US 5,188,963) in view of Moreira (“Efficient removal of PCR inhibitors using agarose-embedded DNA preparations”) and further in view of Maniatis et al. (*Molecular Cloning; a Laboratory Manual*)

Claims 1, 3–7, and 10 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Stapleton (US 5,188,963) in view of Moreira (“Efficient removal of PCR inhibitors using agarose-embedded DNA preparations,” *Nucleic Acids Research*. 1998. Vol. 26, No. 13: Pages 3309–3310) and further in view of Maniatis et al, *Molecular Cloning; a Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1982): pages 150–152. This rejection is respectfully traversed. To warrant rejection under 35 U.S.C. § 103(a), all the claim limitations must be taught or suggested by the prior art. *See* MPEP § 2142.

Applicant maintains the belief that the previously presented claim 1 is not obvious over the cited references without the benefit of impermissible hindsight based upon Applicant’s disclosure. Nonetheless, in the interests of advancing prosecution, Applicant has amended claim 1. Claim 1 is now limited to a method wherein the sieving medium is in a channel of a microfluidic device. The sieving medium is initially unpolymerized and is polymerized after thermocycling is completed. The resulting PCR products are then separated by flowing them through the polymerized sieving medium. Support for the sieving medium being within a channel of a microfluidic device can be found, for example, on page 13, lines 1–4 of paragraph 0057. Support for the sieving medium being initially unpolymerized and then polymerized following thermocycling can be found, for example, on page 13, lines 3 and 4 of paragraph 0057. Thus, no new matter is added by the amendment of the claim.

With regard to amended claim 1, at a minimum, the combination of Stapleton, Moreira, and Maniatis et al. does not teach a sieving medium that is unpolymerized during PCR and then polymerized prior to separating the PCR products by flowing them through the

polymerized sieving medium. Further, Stapleton, Moreira, and Maniatis et al. teach regarding slab gels and so do not teach a sieving medium in a channel of a microfluidic device.

Stapleton teaches “a subdivided matrix” for amplification and separation. *See* column 14, line 12. Amplification **54** and separation **56** submatrices are of “different” compositions. Amplification submatrix **54** is described as being a “preformed” matrix. *See* column 14, line 48. Separation submatrix **56** is described as “comprising a 5% T wedge rehydrated polyacrylamide gel...” *See* column 15, lines 2–8. Clearly the preformed amplification matrix is not polymerized before separating the amplification products in the same matrix. Further, in column 14, lines 51–53, Stapleton teaches that PCR reaction components are “immobilized in sections **54** at the time of matrix-carrier manufacture.” Therefore, Stapleton also does not teach mixing one or more PCR reaction components with an unpolymerized sieving medium in a channel of a microfluidic device.

Moreira teaches different thermocycling and separating matrices. Purified gDNA is thermocycled in agarose blocks having concentrations “as high as 0.3%.” *See* page 3309, paragraph beginning at the bottom of column 1. Following thermocycling, the products are “electrophoresed on 1.2% agarose gels.” *See* page 3310, the second full paragraph. Thus, Moreira, like Stapleton, is silent with regard to an initially unpolymerized sieving medium that is polymerized after thermocycling is completed within the sieving medium.

Maniatis et al. is cited only for teaching that agarose gels having a concentration less than about 0.4% are used for electrophoretic separation of DNA molecules. No mention is made of thermocycling in the gel or polymerizing the gel after thermocycling is completed.

Therefore, the combination cited by the Examiner does not teach or suggest all of the limitations of amended claim 1. Withdrawal of the rejection of claim 1 under 35 U.S.C. § 103(a) as being unpatentable over Stapleton (US 5,188,963) in view of Moreira (“Efficient removal of PCR inhibitors using agarose-embedded DNA preparations”) and further in view of Maniatis et al. (“Molecular cloning; a laboratory manual”) is respectfully requested.

Claims 3–7 and 10 depend directly or indirectly from claim 1. Any claim depending from a nonobvious claim is also nonobvious. *See* MPEP § 2143.03 and *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Therefore, dependent claims 3–7 and 10 are

nonobvious. Withdrawal of the rejections of these claims as being unpatentable over Stapleton in view of Moreira is also respectfully requested. Applicant wishes to point out that dependent claims 3, 5, and 6 have been amended to conform the terminology of these claims to amended claim 1. Claim 10 has been amended to depend from claim 1 rather than from claim 9. No new matter is added by the amendments to these claims.

II. Claim rejections under 35 U.S.C. § 103(a) as being unpatentable over Stapleton (US 5,188,963) in view of Moreira (“Efficient removal of PCR inhibitors ...”) and further in view of Maniatis et al. (“Molecular cloning; a laboratory manual”) and Woolley et al. (“Ultra-high-speed DNA fragment separations using microfabricated capillary array electrophoresis chips”)

Claims 8 and 9 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Stapleton (US 5,188,963) in view of Moreira (“Efficient removal of PCR inhibitors using agarose-embedded DNA preparations”) and further in view of Maniatis et al. (*Molecular Cloning; A Laboratory Manual*) and Woolley et al. (“Ultra-high-speed DNA fragment separations using microfabricated capillary array electrophoresis chips,” Proc. Natl. Acad. Sci. November 1994. Vol. 91: Pages 11348–11352). This rejection is respectfully traversed.

As demonstrated above, Applicant’s claim 1 is nonobvious. Claims 8 and 9 depend directly and indirectly, respectively, from claim 1. As any claim depending from a nonobvious claim is also nonobvious, dependent claims 8 and 9 are nonobvious. Further, while Woolley et al. teach separating PCR amplification products within a microfluidic device, they do not teach mixing PCR reaction components with an unpolymerized sieving medium and then polymerizing the sieving medium after thermocycling of the included PCR reaction components is completed. The sample separated in the microfluidic device of Woolley et al. is amplified outside of the device, “precipitated with ethanol and then resuspended in 1 mM Tris/0.1 mM EDTA, pH 8.2, prior to injection” into the device. *See* page 11349, column 2, lines 39–41. Further, the separation channel of the microfluidic device appears to be filled with a separation buffer that is not polymerized. *See* page 11349, column 2, lines 16–26. Only the coating applied to channel surfaces are polymerized. *See* page 11349, column 2, lines 9–16. Withdrawal of the

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rejection of claims 8 and 9 under 35 U.S.C. § 103(a) as being unpatentable over Stapleton in view of Moreira and further in view of Maniatis et al. and Woolley et al. is, therefore, respectfully requested.

Conclusion

For the foregoing reasons, Applicant believes all the pending claims are in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned attorney.

Respectfully submitted,



Ann C. Petersen
Reg. No. 55,536

CALIPER LIFE SCIENCES, INC.
605 Fairchild Drive
Mountain View, CA 94043
Direct: 650-623-0667
Fax: 650-623-0504
ann.petersen@caliperLS.com